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     (FILE 'HOME' ENTERED AT 14:23:27 ON 23 MAY 2007)

     FILE 'CASREACT' ENTERED AT 14:23:44 ON 23 MAY 2007
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L3             3 S L1 FULL

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L1               STR
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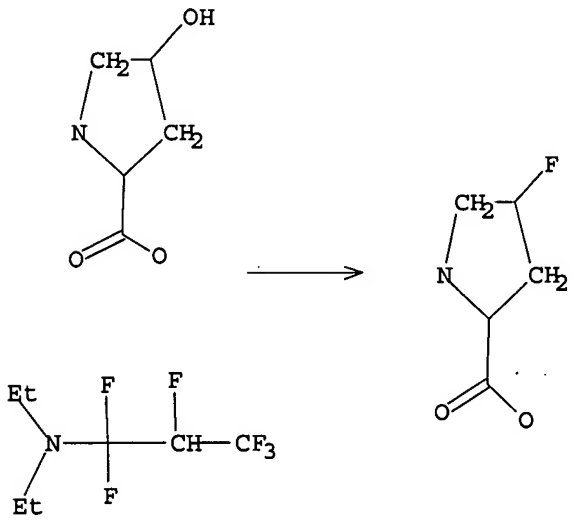


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SEARCH TIME: 00.00.01


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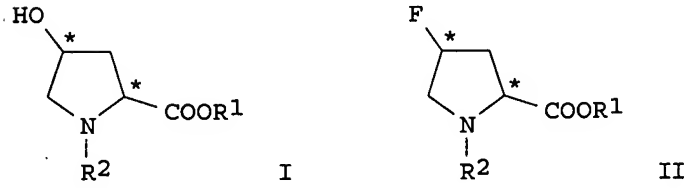
L3 ANSWER 1 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
AN 145:397782 CASREACT
TI Process for production of optically active fluoroproline derivative
IN Kondo, Norihisa; Watanabe, Akio; Kanezaki, Hiroki; Kawada, Kosuke
PA Tosoh F-Tech, Inc., Japan
SO PCT Int. Appl., 23pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006103986	A1	20061005	WO 2006-JP305674	20060322

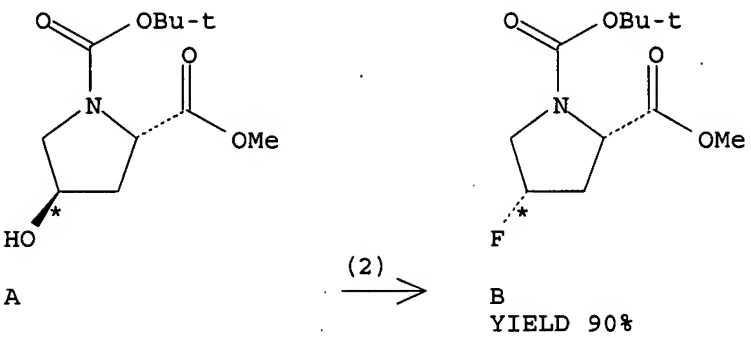
PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI JP 2005-92878 20050328
OS MARPAT 145:397782
GI



AB There is provided a process for producing an optically active fluoroproline derivative represented by the general formula (I; R1 = substituted or unsubstituted alkyl or aryl group; R2 = substituted or unsubstituted alkyl, aryl, alkylcarbonyl, alkoxycarbonyl, arylcarbonyl or aryloxycarbonyl group; an asterisk (*) denotes an asym. carbon) by fluorinating an optically active hydroxyproline derivative represented by the general formula (II; R1 , R2 = same as above). The process comprises adding N-(2-chloro-1,1,2-trifluoroethyl) diethylamine (CTT) or N-(1,1,2,3,3,3-hexafluoropropyl)diethylamine (PPDA) which is inexpensive and easy to handle to an aprotic nonpolar organic solvent at a temperature of 10° or lower and then fluorinating the compound I at a temperature ranging from 10 to 50°. This process enables to produce an optically active fluoroproline derivative represented by the general formula II in which the configuration at position-4 of a compound represented by the general formula I is inverted, in a high purity with reduced production of byproducts, e.g. chloroproline derivs. when CTT is used as the fluorinating agent. Thus, 4.91 g N-(tert-butoxycarbonyl)-(2S,4R)-4-hydroxyproline Me ester and 0.14 g ethanol were dissolved in 18 g CHCl3, cooled to -10°, followed by adding 4.55 g CTT, and the reaction liquid was warmed to 30°, and stirred for 15 h to give 89% N-(tert-butoxycarbonyl)-(2S,4S)-4-fluoroproline Me ester (97.8% purity).

RX(2) OF 2 A ===> B



A

B
YIELD 90%

RX(2) RCT A 74844-91-0
RGT F 309-88-6 Ishikawa reagent
PRO B 203866-16-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C -> 10 deg C
SUBSTAGE(2) 20 hours, 50 deg C
NTE fluorination

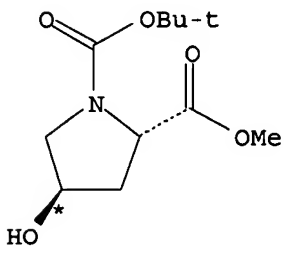
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
AN 142:261782 CASREACT
TI Process for preparation of cis-4-fluoro-L-proline derivatives
IN Tomisawa, Kazuyuki; Tatsuta, Dai; Yoshida, Tomomichi; Yokoo, Chihiro
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005016880	A1	20050224	WO 2004-JP11827	20040818
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004265182	A1	20050224	AU 2004-265182	20040818
	CA 2534884	A1	20050224	CA 2004-2534884	20040818
	EP 1657237	A1	20060517	EP 2004-771788	20040818
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1839120	A	20060927	CN 2004-80023726	20040818
	NO 2006000703	A	20060313	NO 2006-703	20060214
	US 2006281927	A1	20061214	US 2006-568708	20060804
PRAI	JP 2003-207718		20030818		
	WO 2004-JP11827		20040818		

OS MARPAT 142:261782
AB This invention pertains to a method for producing high purity cis-4-fluoro-L-proline derivs., which comprises reacting a trans-4-hydroxy-L-proline derivative with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in the presence of a HF scavenger. For example, (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid Me ester was reacted with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in CH2Cl2 in the presence of NaF to give (2S,4S)-1-(tert-butoxycarbonyl)-4-fluoropyrrolidine-2-carboxylic acid Me ester. This invention provides a convenient method to prepare cis-4-fluoro-L-proline derivs. in high yield under mild conditions at low cost.

RX(1) OF 29 A + B ===> C...



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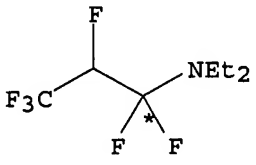

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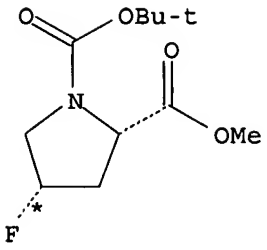

C
YIELD 85%

RX(1) RCT A 74844-91-0, B 309-88-6
RGT D 7681-49-4 NaF
PRO C 203866-16-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 20 hours, room temperature
NTE alternative prepn. shown
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
AN 129:202944 CASREACT
TI Preparation of intermediates and 1,3-dioxo-1H-pyrrolo[1,2-c]imidazoles
IN Taylor, Eric Deguyon; Petrov, Viacheslav Alexandrovich; Schaefer, Matthias; Drauz, Karlheinz; Vogt, Anne; Weckbecker, Christoph; Swearingen, Steven H.; Kamireddy, Balreddy
PA E. I. Du Pont de Nemours & Co., USA; Degussa A.-G.
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9837065	A1	19980827	WO 1998-US2721	19980213
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	IN 1998CA00208	A	20051118	IN 1998-CA208	19980209
	ZA 9801168	A	19990812	ZA 1998-1168	19980212
	CA 2276056	A1	19980827	CA 1998-2276056	19980213
	AU 9861604	A	19980909	AU 1998-61604	19980213
	EP 973739	A1	20000126	EP 1998-906363	19980213
	EP 973739	B1	20051102		
	R: DE, FR, IT				
	BR 9807256	A	20000502	BR 1998-7256	19980213
	US 6384234	B1	20020507	US 1999-367899	19991230
	US 2002137946	A1	20020926	US 2002-35136	20020104
	US 6664400	B2	20031216		
PRAI	US 1997-38429P	19970219			
	WO 1998-US2721	19980213			
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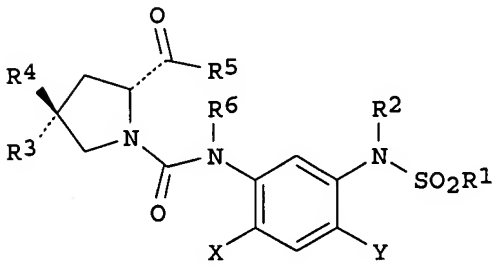
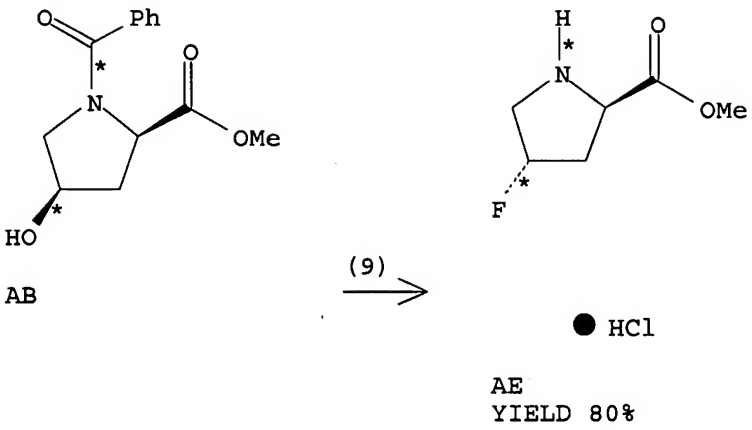
OS MARPAT 129:202944
GI



I

AB Title compds. [I; R1 = haloalkyl, alkoxyalkyl, cyanoalkyl, etc.; R2 = H, (halo)alkyl, alkanoyl, alkoxycarbonyl, etc.; R3 = H or OH; R4,X = H, F, Cl; Y = F or Cl; R5 = OH; R6 = H; R5R6 = bond] were prepared Thus, N-(2-chloro-4-fluoro-5-isocyanatophenyl)chloromethanesulfonamide (preparation given) was amidated by cis-4-hydroxy-D-proline to give I (R1 = Y = Cl, R2 = H, X = F)(II; R4 = R6 = H, R3 = R5 = OH) which was cyclized and the product fluorinated to give II (R3 = H, R4 = F, R5R6 = bond).

RX(9) OF 34 ...AB ===> AE...



YIELD 80%

RX(9) RCT AB 212198-48-6

STAGE(1)
RGT W 309-88-6 Ishikawa reagent
SOL 75-09-2 CH2Cl2, 108-88-3 PhMe

STAGE(2)
RGT I 7647-01-0 HCl
SOL 7732-18-5 Water

PRO AE 131176-03-9

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L6             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  "YOSHIDA TOMOMICHI"/AU
L7            61 SEA FILE=CAPLUS ABB=ON  PLU=ON  "YOKOO CHIHIRO"/AU
L8           150 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 OR L5 OR L6 OR L7
L9             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (FLUORO(L)PROLINE OR
                 FLUOROPROLINE OR FLUORO(W)PROLINE)

=> d bib abs
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L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:158636 CAPLUS
DN 142:261782
TI Process for preparation of cis-4-fluoro-L-proline derivatives
IN Tomisawa, Kazuyuki; Tatsuta, Dai; Yoshida, Tomomichi; Yokoo, Chihiro
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005016880	A1	20050224	WO 2004-JP11827	20040818
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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	AU 2004265182	A1	20050224	AU 2004-265182	20040818
	CA 2534884	A1	20050224	CA 2004-2534884	20040818
	EP 1657237	A1	20060517	EP 2004-771788	20040818
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1839120	A	20060927	CN 2004-80023726	20040818
	NO 2006000703	A	20060313	NO 2006-703	20060214
	US 2006281927	A1	20061214	US 2006-568708	20060804
PRAI	JP 2003-207718	A	20030818		
	WO 2004-JP11827	W	20040818		

OS CASREACT 142:261782; MARPAT 142:261782
AB This invention pertains to a method for producing high purity cis-4-fluoro-L-proline derivs., which comprises reacting a trans-4-hydroxy-L-proline derivative with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in the presence of a HF scavenger. For example, (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid Me ester was reacted with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in CH2Cl2 in the presence of NaF to give (2S,4S)-1-(tert-butoxycarbonyl)-4-fluoropyrrolidine-2-carboxylic acid Me ester. This invention provides a convenient method to prepare cis-4-fluoro-L-proline derivs. in high yield under mild conditions at low cost.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his full

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     FILE 'CASREACT' ENTERED AT 14:23:44 ON 23 MAY 2007
L1             STRUCTURE UPLOADED
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L3           3 SEA SSS FUL L1 (    10 REACTIONS)
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               E TATSUTA DAI/AU
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L6           2 SEA ABB=ON  PLU=ON  "YOSHIDA TOMOMICHI"/AU
               E YOKOO CHIHIRO/AU
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L8         150 SEA ABB=ON  PLU=ON  L4 OR L5 OR L6 OR L7
L9           1 SEA ABB=ON  PLU=ON  L8 AND (FLUORO(L)PROLINE OR FLUOROPROLINE
               OR FLUORO(W)PROLINE)
               D QUE L9 STAT
               D BIB ABS


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     FILE CASREACT
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     FILE CONTENT:1840 - 19 May 2007 VOL 146 ISS 22

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     database compiled under the direction of Professor Dr. Klaus Kieslich.

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     identification.

     FILE CAPLUS

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FILE LAST UPDATED: 22 May 2007 (20070522/ED)

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